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L1: Entry 1 of 1

File: USPT

Aug 10, 1999

DOCUMENT-IDENTIFIER: US 5935927 A

TITLE: Compositions and methods for stimulating amyloid removal in amyloidogenic diseases using advanced glycosylation endproducts

US Patent No. (1):  
5935927Brief Summary Text (11):

In the absence of increased soluble .beta.AP in most cases of AD, the question remains how amyloid accumulates to a greater degree at different rates. Synthetic .beta.APs corresponding to the first 28, 40, or 42 amino acids of .beta.AP (i.e., .beta.AP 1-28, .beta.AP 1-40 and .beta.AP 1-42, respectively) display concentration-dependent aggregation kinetics in in vitro incubations. Fibrillar aggregates form in vitro and these appear similar to brain .beta.-amyloid fibrils at the morphological level using electron microscopy and at the light microscopy and spectroscopic levels using Congo Red and Thioflavin stains.

Detailed Description Text (33):

The term "antibody" includes any immunoglobulin, including antibodies and fragments thereof that binds a specific epitope, and such general definition is intended to apply herein. The term therefore encompasses polyclonal, monoclonal and chimeric antibodies, the last mentioned described in further detail in U.S. Pat. Nos. 4,816,397 and 4,816,567. Also, an "antibody combining site" is that structural portion of an antibody molecule comprised of heavy and light chain variable and hypervariable regions that specifically bind antigen.

Detailed Description Text (36):

The phrase "monoclonal antibody" in its various grammatical forms refers to an antibody having only one species of antibody combining site capable of immunoreacting with a particular antigen. A monoclonal antibody thus typically displays a single binding affinity for any antigen with which it immunoreacts. An antibody may be prepared having a plurality of antibody combining sites, each immunospecific for a different antigen, e.g., a bispecific (chimeric) antibody.

Detailed Description Text (124):

Hamsters were infected by intracerebral injection with a strain of hamster-adapted murine scrapie. After 300 days, the hamsters were sacrificed, the brains sectioned, and the sections fixed on microscope slides. The fixed sections were treated with 70% formic acid for 10 minutes and washed. The slides were then reacted with rabbit antisera specific for RNase (control antisera), prion protein (PrP; Kascsak et al., 1987, J. Virol. 61:3688-93), and AGE (anti-AGE-RNase antisera, as described in Makita et al., 1992, J. Biol. Chem. 267:5133-38). Each serum was diluted 1:500 prior to incubation with the tissue samples. The reactions were incubated overnight at 4.degree. C. Following reaction with the rabbit antisera, the samples were washed with PBS and reacted with an alkaline phosphatase (AP)-conjugated anti-rabbit antibody. The samples were developed with a fuschin AP substrate (Dako), which produces a red color.

Detailed Description Text (147):

Type II diabetes is characterized by deposits of aggregated amylin peptide in the pancreas. After a concentration-dependent lag period during in vitro incubations, soluble preparations of synthetic amylin slowly form fibrillar aggregates that resemble natural amyloid (Lorenzo et al., 1994, Nature 368:756-760) and are measurable by electron microscopy or by Congo Red birefringence under polarized light (Fraser et al., 1991, Biophys. J. 90:1194-1201). Aggregation of soluble amylin in these in vitro assays

is expected to be enhanced by addition of small amounts of pre-aggregated amylin "seed" material. These seeds have also been prepared herein using a naturally occurring reaction between glucose and protein amino groups resulting in the formation of advanced glycosylation endproducts (AGEs) which chemically crosslink proteins. AGE-modified amylin-nucleation seeds are expected to further accelerate aggregation of soluble amylin compared to non-modified "seed" material. Over time, nonenzymatic advanced glycosylation, which is likely to occur at lysine-1 of amylin, and may occur at arginine-10, also results in the gradual accumulation of a set of post-translational covalent adducts on long-lived proteins in vivo. Using a standardized competitive ELISA assay, plaque fractions of Type II pancreatic islet cells are expected to be found to contain more AGE adducts per mg protein than found in like preparations from healthy, age-matched controls. These results indicate that the in vivo half-life of amylin is prolonged in Type II diabetes, resulting in greater accumulation of AGE modifications, which in turn can act to promote accumulation of additional amyloid.

L1 ANSWER 17 OF 59 MEDLINE on STN  
 AN 97260239 MEDLINE  
 DN 97260239 PubMed ID: 9106334  
 TI Transplant rejection associated with the presence of human leucocyte antigen **antibodies** detected by the **Fc** gamma R inhibition test but not by the **lymphocytotoxicity** test.  
 AU Neppert J; Claas F H; Persijn G G; Washington G; Tapken A  
 CS Institute of Transfusion Medicine, University Hospital Kiel, Germany.  
 SO TRANSPLANT IMMUNOLOGY, (1997 Mar) 5 (1) 45-8.  
 Journal code: 9309923. ISSN: 0966-3274.  
 CY ENGLAND: United Kingdom  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 199706  
 ED Entered STN: 19970620  
 Last Updated on STN: 19970620  
 Entered Medline: 19970612  
 AB The unselected sera from 869 human leucocyte antigen (HLA) immunized patients awaiting a kidney transplant were analysed using the complement-dependent **lymphocytotoxicity** test (LCT) with peripheral mononuclear blood cells and the complement-independent immune **phagocytosis** inhibition test (IPI) with monocytes derived from between five and 10 donors. Sera from 659 patients were LCT and IPI negative when tested against this small panel. Seventy-nine patients had HLA immunoglobulin-G (IgG) **antibodies**, detectable by the IPI only. Sera from 117 patients had concordantly positive IPI and LCT reactivity with cells from certain donors and concordantly negative IPI and LCT reactivity with cells from other donors (no isolated IPI and no isolated LCT reactions). Fourteen patients had a mixed type of reactivity. Laboratory findings were interpreted along with the transplantation history of the respective patients. Group 1 comprised patients for whom negative results were obtained in both the LCT and the IPI; group 2 patients who were also LCT negative but IPI positive. These two groups showed a significantly different history with respect to the number of irreversible immunological transplant rejections. In group 1, 25.3% of the transplanted kidneys had been rejected whereas in group 2, 56.0% of the kidneys had been rejected ( $p = 5 \times 10^{-5}$ ). The high incidence of rejections in the group showing only IPI reactions was comparable with that of group 4 comprising patients with concordant IPI and LCT reactions (59.4%). It is inferred from this retrospective study that renal allograft rejection is associated with the development of IPI reactive **antibodies** which are not detectable by the LCT. The presence of these **antibodies** prior to transplantation could be detrimental to the transplanted organ. This being the case, the incidence of transplant failures could be reduced by pretransplant **screening** using the IPI and by avoiding crossmatch positive donors identified by IPI, especially in patients waiting for a retransplantation.

L10 ANSWER 13 OF 18 MEDLINE on STN  
 AN 90063673 MEDLINE  
 DN 90063673 PubMed ID: 2685183  
 TI Immunotoxins: a clinical review of their use in the treatment of malignancies.  
 AU Hertler A A; Frankel A E  
 CS Section of Hematology, Louisiana State University Medical Center, Shreveport.  
 SO JOURNAL OF CLINICAL ONCOLOGY, (1989 Dec) 7 (12) 1932-42. Ref: 100  
 Journal code: 8309333. ISSN: 0732-183X.  
 CY United States  
 DT (CLINICAL TRIAL)  
 Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)  
 LA English  
 FS Priority Journals  
 EM 199001  
 ED Entered STN: 19900328  
 Last Updated on STN: 19900328  
 Entered Medline: 19900110  
 AB Immunotoxins are a new class of antitumor agents consisting of tumor-selective ligands (generally monoclonal **antibodies** [MoAbs]) linked to highly toxic protein molecules that have been modified to remove their normal **tissue**-binding domains. These immuno-conjugates combine the potency of the parent toxin with the specificity of the attached ligand. Toxins used in the construction of immunotoxins belong to a group of peptides that catalytically inhibit the elongation step of protein synthesis, and include ricin, abrin, pokeweed antiviral protein, gelonin, Pseudomonas exotoxin A, diphtheria toxin, and alpha-sarcin. To synthesize immunotoxins, the normal cell-binding function must be removed by chemical cleavage or modification, or in the case of toxins that have been cloned, genetic engineering used to delete amino acids critical to cell binding. Covalent linkage of toxin to ligand generally involves a disulfide or thioether bond, though recently, recombinant toxin molecules with ligands that are genetically engineered into the protein have been made. The most successful clinical application of immunotoxins has been in the depletion of T cells from allogeneic bone marrow grafts to prevent **graft-versus-host** disease (GVHD). Clinical trials have been conducted using immunotoxins for the systemic treatment of chronic lymphocytic leukemia (CLL), GVHD, and selected solid tumors. With the possible exception of GVHD, responses have been limited. Obstacles have included rapid systemic **clearance**, poor delivery to extravascular tumor deposits, and humoral immune responses to the immunotoxin. Research to overcome these problems is in progress and should lead to a better definition of the role of immunotoxins in the therapy of malignancies.

L10 ANSWER 17 OF 18 MEDLINE on STN  
 AN 85041465 MEDLINE  
 DN 85041465 PubMed ID: 6208658  
 TI Chimerism in skin of bone marrow transplant recipients.  
 AU Thomas J A; Wakeling W F; Imrie S F; Sloane J P; Powles R L; Lawler S D  
 SO TRANSPLANTATION, (1984 Nov) 38 (5) 475-8.  
 Journal code: 0132144. ISSN: 0041-1337.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 198412  
 ED Entered STN: 19900320  
 Last Updated on STN: 19900320  
 Entered Medline: 19841220  
 AB Skin biopsies from 3 patients receiving one-haplotype-matched bone marrow grafts have provided a unique opportunity to demonstrate the presence of donor cells in situ using immunohistological techniques and a monoclonal **antibody** directed against an epitope common to HLA-A2 and HLA-A28 antigens. The infiltrating cells were also analyzed in consecutive **tissue** sections with a panel of monoclonal **antibodies** to human leukocyte antigens, T cells, and epidermal Langerhans cells. Most of the infiltrating cells were shown to be T lymphocytes of donor origin, regardless of whether the histological changes were consistent with **graft-versus-host** disease (GVHD) or were eczematous. Donor T cells were also shown to colonize histologically normal skin soon after transplantation. Epidermal keratinocytes, dermal endothelium, and adnexal structures did not express the donor HLA type (i.e., were host derived) but the origin of the epidermal Langerhans cells could not **clearly** be established. The data show that donor cells preferentially migrate to certain sites in skin after transplantation and are not always associated with GVHD.

L10 ANSWER 18 OF 18 MEDLINE on STN  
 AN 83172880 MEDLINE  
 DN 83172880 PubMed ID: 6340277  
 TI Antilymphocytic **antibodies** and marrow transplantation. VI.  
 Absence of immunosuppression in vivo after injection of monoclonal **antibodies** blocking **graft-versus-host** reactions and humoral **antibody** formation in vitro.  
 AU Thierfelder S; Hoffmann-Fezer G; Rodt H; Doxiadis I; Eulitz M; Kummer U  
 SO TRANSPLANTATION, (1983 Mar) 35 (3) 249-54.  
 Journal code: 0132144. ISSN: 0041-1337.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 198305  
 ED Entered STN: 19900318  
 Last Updated on STN: 19900318  
 Entered Medline: 19830527  
 AB The in vivo and in vitro effectiveness of several monoclonal antimouse T and B cell **antibodies**, of anti-Th-1 and of Iak serum, as well as of ATG were compared. The parameters were prolongation of skin graft survival, prevention of **graft-versus-host** disease (GVHD), **antibody** and primary and secondary plaque formation against sheep redblood cells (RBCs), and T cell depletion of lymphoid **tissues**. In general, in vitro effectiveness of the monoclonal **antibodies** exceeded their in vivo effectiveness. Skin graft survival was prolonged by ATG, but not by monoclonal anti-T, or anti-T plus anti-B **antibody**. GVHD was prevented by in vitro

incubation of donor bone marrow with monoclonal anti-Th-1, but in vivo treatment of marrow donors was ineffective. Treatment with ATG was successful. Anti Iak **antibody** blocked plaque formation by spleen cells incubated with sheep RBCs, but had no effect on secondary plaque formation when given in vivo. Neither was there any in vivo effect of anti-Iak or anti-Th-1 on antisheep RBC agglutinin formation. ATG was effective in both of these assays, although its cytotoxic and complement-fixing titer did not exceed that of anti-Th-1 or anti-Iak. Although anti-Th-1 was **cleared** more rapidly from the serum of mice expressing the corresponding Th-1 alloantigen, than from mice with the noncorresponding alloantigen and although anti-Th-1 was shown to bind to the T cell areas of the lymphoid **tissue**, it did not--unlike ATG--deplete these areas of T cells. Possible reasons for the difference in effectiveness of in vitro and in vivo application of these monoclonal **antibodies** are discussed.

=>

L3 ANSWER 25 OF 33 MEDLINE on STN  
 AN 88059564 MEDLINE  
 DN 88059564 PubMed ID: 3316274  
 TI Role of fibronectin on the **clearance** and **tissue** uptake  
 of antigen and immune complexes in rats.  
 AU Cosio F G; Bakaletz A P  
 CS Department of Medicine, Ohio State University, Columbus 43210.  
 SO JOURNAL OF CLINICAL INVESTIGATION, (1987 Nov) 80 (5) 1270-9.  
 Journal code: 7802877. ISSN: 0021-9738.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Abridged Index Medicus Journals; Priority Journals  
 EM 198712  
 ED Entered STN: 19900305  
 Last Updated on STN: 19900305  
 Entered Medline: 19871223  
 AB In the present study, we have evaluated how plasma fibronectin (FN) and **tissue** FN can affect the **clearance** from the circulation and organ uptake of antigen or immune complexes (IC) that have the capacity to bind to FN. Phenylated gelatin (DNP-GL) (a FN binding antigen) and IC composed of DNP-GL and monoclonal IgG1 anti-dinitrophenol (DNP) **antibodies** were tested. These probes were compared with DNP-bovine serum albumin (BSA) (a non-FN-binding antigen) and DNP-BSA IC formed with the same anti-DNP **antibody** used for the preparation of DNP-GL IC. We found evidence that DNP-GL, but not DNP-BSA, formed complexes with soluble FN in vitro and the data strongly suggest that DNP-GL-FN complexes form in vivo. The formation of complexes with plasma FN aided in the clearance of DNP-GL from the circulation, as shown by the facts that DNP-GL was removed from the circulation much faster than DNP-BSA and that complexes of DNP-GL with plasma FN were removed from the circulation faster than uncomplexed DNP-GL. The sites of deposition of DNP-GL were also different from those of DNP-BSA. Thus, DNP-GL demonstrated higher hepatic, splenic, and renal uptake than did DNP-BSA. Renal uptake of DNP-GL was quite high despite the fact that DNP-GL is anionic. Indeed, expressed per gram of tissue, liver and kidney deposition of DNP-GL was not significantly different. By immunofluorescence microscopy, DNP-GL could be demonstrated in hepatic sinusoids and glomerular mesangium. In vitro, DNP-GL bound to FN in the mesangium of frozen sections of kidney tissue. IC formed with DNP-GL or DNP-BSA demonstrated virtually the same size, yet the fate of DNP-GL IC was strikingly different from that of DNP-BSA IC. The removal of DNP-GL IC from the circulation was mediated by the antigen and not by **Fc** receptors since gelatin (an inhibitor of DNP-GL clearance) but not aggregated IgG (an inhibitor of **Fc** receptors) inhibited the removal of DNP-GL IC from the circulation. In summary, these studies suggest that the ability of an antigen or IC to bind to FN markedly influences the fate of that antigen or IC. Specifically, binding to FN accelerates clearance from the circulation and favors hepatic and renal (primarily mesangial) uptake of the FN binding antigen or IC.

L3 ANSWER 18 OF 33 MEDLINE on STN  
 AN 91209403 MEDLINE  
 DN 91209403 PubMed ID: 2019290  
 TI Targeting behavior of rat monoclonal IgG **antibodies** in vivo:  
 role of **antibody** isotype, specificity and the target cell  
 antigen density.  
 AU Yousaf N; Howard J C; Williams B D  
 CS Department of Rheumatology, University Hospital of Wales, Babraham,  
 Cambridge.  
 NC CA 34913 (NCI)  
 SO EUROPEAN JOURNAL OF IMMUNOLOGY, (1991 Apr) 21 (4) 943-50.  
 Journal code: 1273201. ISSN: 0014-2980.  
 CY GERMANY: Germany, Federal Republic of  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 199105  
 ED Entered STN: 19910616  
 Last Updated on STN: 19910616  
 Entered Medline: 19910530  
 AB The studies described in this report were designed to investigate factors  
 that could influence the behavior of erythrocytes following their  
 interaction with monoclonal **antibodies** (mAb) in a fully  
 homologous experimental opsonization system in vivo. The  
**clearance** profiles and **tissue** distribution of target  
 erythrocytes were examined in both normal and de complemented rats  
 preinjected with rat IgG2a or IgG2b mAb directed against the same or  
 different sites on RT1Aa, the classical class I major histocompatibility  
 complex antigen of the DA rat. Complement played a major role in  
 augmenting the clearance and promoting hepatic sequestration of target  
 erythrocytes in rats preinjected with IgG2a mAb directed against the S  
 site. In contrast, an intact complement system was not an essential  
 requirement for erythrocyte clearance when S site-specific IgG2b mAb were  
 used. With each **antibody** tested, (DA x PVG)F1 cells, expressing  
 about half as much antigen, were removed significantly slower than DA  
 erythrocytes, this finding being more pronounced when the animals had been  
 preinjected with mAb of the IgG2a isotype. A comparison of the tissue  
 distribution of DA and (DA x PVG)F1 erythrocytes indicated that hepatic  
 uptake was greater for target cells expressing higher antigen density. A  
 considerable degree of heterogeneity was observed in the in vivo behavior  
 of the target erythrocytes with three groups of IgG2b mAb that recognized  
 different sites on the class I molecule. The S site-specific IgG2b mAb  
 were much more efficient in the hepatic **Fc** receptor-mediated  
 clearance system than were the P site-directed mAb of the same subclass.  
 Our results suggest that **antibody** specificity may also be a  
 contributory factor, in addition to **antibody** isotype and target  
 cell antigen density, in determining the fate of target cells in vivo.



L8 ANSWER 4 OF 7 MEDLINE on STN  
AN 2000150830 MEDLINE  
DN 20150830 PubMed ID: 10688122  
TI Single amino acid substitution in the **Fc** region of chimeric  
TNT-3 **antibody** accelerates **clearance** and improves  
immunoscintigraphy of solid **tumors**.  
AU Hornick J L; Sharifi J; Khawli L A; Hu P; Bai W G; Alauddin M M; Mizokami  
M M; Epstein A L  
CS Department of Pathology, University of Southern California School of  
Medicine, Los Angeles 90033, USA.  
SO JOURNAL OF NUCLEAR MEDICINE, (2000 Feb) 41 (2) 355-62.  
Journal code: 0217410. ISSN: 0161-5505.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 200003  
ED Entered STN: 20000330  
Last Updated on STN: 20000330  
Entered Medline: 20000322  
AB Recent studies in **antibody** catabolism have identified residues  
at the CH2-CH3 interface of the IgG heavy chain critical for serum  
persistence of immunoglobulins. Amino acid substitutions in the  
**Fc** region of murine IgG1 were shown to drastically accelerate  
**antibody** clearance in mice. Our laboratory has previously  
described a human-mouse chimeric TNT-3 (chTNT-3) **monoclonal**  
**antibody** directed against a universal nuclear antigen that has  
potential for the radioimmunotherapy of many solid tumors. In the current  
study, we engineered a chTNT-3 mutant containing a single amino acid  
substitution, to determine whether a more rapid clearance profile would  
make the **antibody** suitable for diagnostic imaging. METHODS: A  
single amino acid substitution in the CH2 domain of the human gamma1  
constant region was made by polymerase chain reaction mutagenesis.  
High-level expression was achieved using the Glutamine Synthetase Gene  
Amplification System, and the chTNT-3 mutant was purified by protein A  
affinity and ion-exchange chromatography. A radioimmunoassay was  
performed to examine antigen binding, and in vivo studies were undertaken  
to evaluate **clearance** and **tumor** targeting in human  
**tumor** xenograft models. RESULTS: The chTNT-3 mutant retained the  
high affinity of chTNT-3, with a binding constant of  $1.5 \times 10^{-9}$  mol/L.  
The mutant was eliminated rapidly from BALB/c mice, with a beta-phase  
half-life of 33.8 h, compared to 134.2 h for chTNT-3. Moreover,  
biodistribution studies in human colon **tumor**-bearing nude mice  
reflected this accelerated **clearance**. Tumor levels of the  
mutant were, respectively, 65%, 39%, and 36% of the tumor levels achieved  
with the parental chTNT-3 6, 12, and 24 h postinjection. The rapid  
clearance of the chTNT-3 mutant from the blood resulted in higher  
tumor-to-normal organ ratios for many normal tissues. Imaging of  
tumor-bearing mice with  $^{99m}\text{Tc}$ -labeled chTNT-3 mutant demonstrated early  
visualization of tumors in 3 different solid tumor xenograft models.  
CONCLUSION: The accelerated clearance produced by a single amino acid  
substitution in the **Fc** region of chTNT-3 leads to improved  
imaging in tumor-bearing mice. These studies suggest that a rapidly  
clearing **antibody** generated by this approach may be useful for  
the immunoscintigraphy of human tumors.

**WEST**

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L6: Entry 8 of 26

File: USPT

Nov 27, 2001

DOCUMENT-IDENTIFIER: US 6322788 B1

TITLE: Anti-bacterial antibodies and methods of use

Detailed Description Text (4):

Animals usually respond to a bacterial infection by producing antibodies against the bacteria. These antibodies help clear the infection by two general methods. In complement-mediated lysis, components of the complement system (e.g., C1q) bind to the constant region of antibodies attached to the cell wall of the bacteria. This interaction triggers various enzymatic events (e.g., the classical pathway and the alternative pathway) which cause the formation of a membrane attack complex that bores holes through bacterial membranes. These holes disrupt the integrity of the bacterial membrane and thus can result in bacterial death. In opsinization, the constant regions of antibodies coating a bacterium directly or indirectly interact with receptors (e.g., Fc receptors or complement receptors) on a phagocyte (e.g., a macrophage, monocyte, or neutrophil). By increasing the affinity of a phagocyte for a bacterium and/or activating the phagocyte, this interaction facilitates the bacterium being phagocytosed and destroyed by the phagocyte. Unfortunately, complement-mediated lysis and opsinization may not function efficiently when the pathogenic bacteria express Fc-binding proteins. This is likely so because the bacterial Fc-binding protein competes with effector molecules (e.g., complement and Fc receptors) for binding to the constant region of the antibacterial antibodies.

L10 ANSWER 14 OF 18 MEDLINE on STN  
 AN 89001489 MEDLINE  
 DN 89001489 PubMed ID: 2971410  
 TI Skin explant culture as a model for cutaneous **graft-versus-host** disease in humans.  
 AU Dickinson A M; Sviland L; Carey P; Reid M M; Hamilton P J; Pearson A J; Proctor S J  
 CS Department of Haematology, Royal Victoria Infirmary, Newcastle upon Tyne, UK.  
 SO BONE MARROW TRANSPLANTATION, (1988 Jul) 3 (4) 323-9.  
 Journal code: 8702459. ISSN: 0268-3369.  
 CY ENGLAND: United Kingdom  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 198811  
 ED Entered STN: 19900308  
 Last Updated on STN: 19900308  
 Entered Medline: 19881118  
 AB An in vitro skin explant model for **graft-versus-host** disease (GVHD) in humans has been used to study the role of effector T cells in the histological pathogenesis of GVHD. In 11 of 12 experiments **clear** GVHD changes of grades II-IV were induced in HLA-mismatched skin explants cultured with allogeneic T cells sensitized by in vitro mixed lymphocyte culture. The role of effector T cells was investigated by comparing results before and after removal of CD3 positive cells, and CD4 positive and CD8 positive T cell-subsets by **antibody** and complement cytolysis from responder populations. Only total removal of CD3 positive T cells prevented histopathological lesions of GVHD in the skin biopsy specimens. The results also demonstrated that the CD4 positive population caused the greatest degree of GVHD in vitro in skin biopsy specimens and direct infiltration into skin by cells is not required for changes to become evident. These results confirm the early results on animal models and demonstrate the use of the skin explant model as a tool for studying the biology of GVHD in humans.

L2 ANSWER 21 OF 41 MEDLINE on STN  
 AN 90107075 MEDLINE  
 DN 90107075 PubMed ID: 2532576  
 TI The role of Fc gamma receptors in mononuclear phagocyte system function.  
 AU Kimberly R P; Salmon J E; Edberg J C; Gibofsky A  
 CS Division of Rheumatic Diseases, Hospital for Special Surgery, Cornell  
 University Medical College, New York, New York 10021.  
 SO CLINICAL AND EXPERIMENTAL RHEUMATOLOGY, (1989 Sep-Oct) 7 Suppl 3 S103-8.  
 Ref: 51  
 Journal code: 8308521. ISSN: 0392-856X.  
 CY Italy  
 DT Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)  
 LA English  
 FS Priority Journals  
 EM 199002  
 ED Entered STN: 19900328  
 Last Updated on STN: 19900328  
 Entered Medline: 19900213  
 AB Abnormalities in host mechanisms for the handling of immune complexes (IC)  
 may promote both **tissue** deposition of pathogenic complexes and  
 interaction of complexes with other immunocompetent cells. Although  
 immune adherence of complexes to erythrocytes may be decreased in patients  
 with autoimmune disease, the significance of this decrease for overall  
 immune complex handling is unclear since many IC release rapidly from the  
 erythrocytes. Little is known about the role of complement receptors in  
 IC uptake by phagocytes. In contrast, the observations of defective Fc  
 gamma receptor-mediated uptake of IgG ligand-coated erythrocytes (one  
 model for erythrocyte-bound complexes) by fixed **tissue**  
 macrophages in SLE patients demonstrate the role of Fc gamma receptors in  
 the uptake of these complexes. Although partly acquired and related to  
 disease activity in SLE, the Fc-mediated **clearance** defect may  
 also have a genetic component. Inherited differences in Fc gamma function  
 may reflect structural polymorphisms of the involved **Fc**  
**receptors**. The emerging picture of Fc gamma receptor structural  
 diversity - several different receptor families (Fc gamma RI, Fc gamma RII  
 and Fc gamma RIII) each with different isoforms, the potential for  
 different glycoforms and cell anchoring mechanisms, and allelic variations  
 within the isoforms - provides the basis for structure/function  
 relationships which have **clear** implications for autoimmune  
 diseases with abnormal **Fc receptor** function.